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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/733,773	12/08/2000	Joseph P. Noel	SALK2410	2948

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EXAMINER

CLOW, LORI A

ART UNIT PAPER NUMBER

1631

DATE MAILED: 12/23/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

**Application No.**

09/733,773

**Applicant(s)**

NOEL ET AL.

**Examiner**

Lori A. Clow, Ph.D.

**Art Unit**

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 01 October 2003.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-18 is/are pending in the application.
- 4a) Of the above claim(s) 19-28 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-18 is/are rejected.
- 7) ☒ Claim(s) 13-16 and 18 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. §§ 119 and 120**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All   b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.  
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)                      4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)                      5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_                      6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

Applicants' arguments, filed 1 October 2003, have been fully considered but they are not deemed to be fully persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Applicant's election with traverse of Group I is acknowledged. The traversal is on the ground(s) that all three groups require the essential feature of a WW domain crystal. With regard to Group II, the argument is persuasive and the claims will be rejoined. This is not found persuasive with regards to Group III. The methods of Group I do not recite use of the crystal(s) of Group III. The requirement is still deemed proper and is therefore made FINAL.

Claims 1-18 are currently pending.

Applicant's arguments are moot due to the new grounds of rejection set forth below.

### ***Declaration***

The declaration submitted 1 October 2003 is acknowledged. The rejection over Verdecia et al. has been withdrawn.

### ***Claims Objections***

Claims 13-16 are objected to under 37 CFR 1.75 as being substantial duplicates of claim 1. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim

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to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). While claims 13-16 do not recite steps identified as (a)-(d) as in claim 1, the recited limitations of each of claims 13-16 are the same as the steps recited in claim 1.

Claim 18 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 17. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Claim 18 comprises the same limitations as set forth in claim 17.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 13 are unclear as to the parameters for defining an interaction site based on atomic coordinates. What are the steps that are necessary to define the metes and bounds of “define” and “based on”? How does one define an interaction site? Furthermore, what is the relationship between steps (a)-(d)? Is this a virtual method or a physical method or both?

Further, claim 1 is unclear in what is meant by a WW domain. What WW domain? Applicant is advised that the specification only supports the Pin1 WW domain.

It is unclear what limitation is intended by claim 9. Is claim 9 limiting the method of claim 1 or is it limiting the actual binding agent?

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

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Claims 1-6 and 8, 9, and 11-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Raganathan et al. (Cell (1997) Vol.89, pages 875-886; PTO 1449 Reference A24) in view of Lu et al. (US 6,495,376).

The present claims are directed to a method of identifying a WW domain binding agent comprising defining an interaction site based on atomic coordinates obtained from a WW domain crystallized in co-complex with a known WW domain binding agent, substrate, or inhibitor; modeling a potential binding agent that fits the interaction site; contacting the potential binding agent with the WW domain; and determining the ability of the potential binding agent to compete with said WW domain substrate for binding to the WW domain.

Raganathan et al. do disclose both structural and functional analyses of Pin1 (instant claim 2), which is a WW domain containing protein (see abstract). They describe in depth the overall architecture and domain topology of Pin1, which consists of two structural domains organized around a hydrophobic cavity (page 876, column 2-page 877, column 1), the surface structure properties (page 877, column 2-page 878), the substrate specificity (page 880, column 1-2), and the reaction mechanism (page 880, bottom column 2-page 883, column 2). A crystal structure of Pin1 complexed with a dipeptide is disclosed, as in step (a) of claim 1. Further, computer generated (MOLSCRIPT, Raster3D and RIBBONS software) ribbon models of Pin1 detailing the PPIase domain and the interdomain cavity (see Figure 1, A and B) are disclosed (claims 9 and 17-18). Raganathan et al. do not disclose contacting binding agents and determining the ability of the agent to bind.

However, Lu et al. teach methods and compositions of WW-domains as phosphoserine and phosphothreonine binding modules. The invention relates to methods of modulating protein-

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protein interactions comprising modulating the binding of WW-domain polypeptides (instant claim 6). The invention also describe molecules which mimic a WW-domain (as required by instant claim 8) (column 2, lines 8-12). The invention further includes a method for modulating the activity of a ligand or ligand-mimic for a WW-domain, or a WW-domain containing polypeptide, wherein the modulation is inhibition or enhancement (column 2, lines 38-45) as in claims 4-5. Furthermore, test substances can act as antagonists or agonists (instant claim 3) (column 3, lines 39-40; column 11, lines 9-17). Furthermore, a WW domain binding agent, NIMA, is disclosed (column 8, lines 27-32) as recited in claim 12. Test substances are added to the WW-domain polypeptide either before or following the addition of the ligand under conditions suitable for maintaining WW-domain and ligand in a conformation appropriate for formation of a combination (column 10, lines 61-65). X-ray and NMR structural analysis are used to identify the salient features of the WW-domain (column 18, lines 23-31). In order to determine the structural basis for binding specificity, mutagenesis, and molecular modeling were performed on the Pin1 crystal structure (see Example 6 beginning column 24). Polypeptides of Lu et al. can be made de novo, as required by instant claim 11 (see, for example, column 9, lines 44-48).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to utilize the WW domain structural and functional information provided by Raganathan et al. to contact a WW domain with its substrate or to contact the WW domain with a potential binding agent, whether it be an agonist, antagonist, inhibitory agent etc., as is done by Lu et al. It is well known in the field of crystallography that modeling programs are used to generate three-dimensional representations of molecules along with their binding partners. It

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would have been obvious to use all of the crystallographic structural and functional information available in the prior art to determine a binding agent of a WW domain. The motivation to do so is provided by Raganathan et al. at page 884, which states:

“Structural studies of Pin1 complexes with native substrates and systematic mutagenesis of Pin1 residues implicated in catalysis and substrate recognition should help resolve the mechanism of Pin1-dependent cell cycle regulation”.

No claims are allowed.

### *Inquiries*

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242, or (703) 308-4028.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lori A. Clow, Ph.D., whose telephone number is (703) 306-5439. The examiner can normally be reached on Monday-Friday from 10 am to 6:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael P. Woodward, Ph.D., can be reached on (703) 308-4028.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Legal Instrument Examiner, Tina Plunkett, whose telephone number is (703) 305-3524, or to the Technical Center receptionist whose telephone number is (703) 308-0196.

*Lori A. Clow*  
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MARJORIE MORAN  
PATENT EXAMINER

*Marjorie A. Moran*